REMARKS

Claim 48 has been amended such that it is dependent upon claim 46 and new claim 75 has been added to further define how the change in the physical work capacity of the subject is monitored. Basis for new claim 75 can be found in the specification, for example at page 18 line 10 to page 20 line 16.

Applicants preserve all rights to file one or more divisional applications for any subject matter disclosed in this application and not presently claimed.

Claim 48 was objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the scope of the subject matter of a previous claim. In response Applicant submits that claim 48 has been appropriately amended.

The claims were rejected under 35 USC 103(a) as allegedly being unpatentable over AU-A-63136/94 and WO 97/16977 both in view of Clark et al. and Ballard et al. (US patent 6,319,522). Applicant respectfully traverses this rejection and submits that the references do not set forth even a *prima facie* case of obviousness for the invention as now claimed.

As stated previously, to establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation to modify the references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or reference when combined) must teach or suggest all the claimed limitations.

Contrary to what the Examiner asserts, Applicants submit that there is no motivation to combine the cited references and no reasonable expectation of success. Furthermore even if the skilled addressee did combine the references there is no combination of the references that disclose or suggest a method of changing the physical work capacity of a subject by administering to the

subject a food composition containing a colostrum fraction prepared as defined in claims 28 and 74.

Applicants submit that the present invention relates to a method wherein a processed colostrum fraction is used to change the physical work capacity of a subject i.e. the measure of the ability to do physical work including any exercise performance, recovery after exercise and reduction of fatigue. The present invention provides a colostrum fraction that preserves a combination of components including antibodies (especially when hyperimmune colostrum is used) which when ingested has the effect of improving the ability to do physical work including exercise and recovering after the exercise. The present invention is not directed to treating infectious conditions which are generally treated by antibodies.

Contrary to the present invention WO97/16977 is not directed to a non-bacterial or non-infectious use. WO97/16977 relates to processing colostrum to maintain colostrum antibodies and the processed product (which may be added to dairy products) is then used to treat infectious conditions. The example on page 10 to 13, table 3 to 6, illustrates that the addition of the processed colostrum had no effect on shelf life and that the colostrum prepared by this process can be safely added to dairy products. No evidence is provided that shows that the product could survive in the gastrointestinal tract (GIT).

Similarly, AU-A-63136/94 relates to a process which preserves proteins such as antibodies in the colostrum and discloses a colostrum preparation to improve antibody content so as to provide antibody enriched colostrum to treat infectious diseases. AU-A-63136/94 also provides an economic process to reduce the problem of salt when colostrum is processed. However, the emphasis is merely to provide colostrum in a form without loss of antibody activity. The perceived use of the product is that of an antibody use for eradicating disease such as bacterial infections. Again contrary to the present invention there is no reference to other uses least of all a use to improve a non-infectious condition such as to improve physical work capacity and recovery from it.

Clark et al. is primarily directed to promoting the benefits of whole colostrum. The Examiner states that Clark et al teaches that colostrum contains IGF-1 and a number of growth factors and states that IGF-1 can improve body composition and suggests that it may be administered via colostrum. However the Applicants submit that this merely indicates that colostrum is a source of IGF-1 and does not provide the skilled addressee of a teaching that processed colostrum can change the physical work capacity of a subject for the following reasons:

The bovine IGF-1 from the bovine colostrum cannot be assumed to have the same systemic effect in the human despite amino acid homology between human and bovine IGF-1. In Read et al. (1986) (copy enclosed) it stated that *"Bovine IGF-1 was 11-19% as effective as human IGF-1 in competing for binding with ^{125}I-labelled human IGF-1..."*. Therefore bovine IGF-1 (and other bovine growth factors which are not all homologous to the human growth factors) could not be expected to elicit the same effects.

Furthermore prior to the present invention it was understood that as a food bovine colostrum must be given orally, and will mostly not survive the acidic/enzymatic environment of the GIT.

Moreover, for the bovine IGF-1 from the orally administered colostrum to have a systemic effect, it is highly unlikely that the concentration delivered in the colostrum would deliver sufficient quantities to have an effect on exercise performance and recovery from that exercise since the IGF-1 must be deliverable to the cells to have an impact. The attached declaration by Jon Buckley includes calculations showing that the possible effect of orally administered IGF-1 on circulating IGF-1 levels in the human is minimal, and not able to be measured given current technology. This conclusion is supported by the results obtained in clinical studies using products made according to the invention.

Furthermore the Examiner states that Clark et al. reduces muscle damage during exercise by enhancing healing (see page 44-45). In response the Applicants submit that Clark et al. merely

points to a reference (Sporn et al.) which discloses that bovine colostrum contained a protein substance that stimulated wound healing and that IFG-1 stimulates cellular growth.

Applicants submit that Clark et al on page 44 (in the paragraphs referred to by the Examiner) refers to the discovery that "bovine colostrum contained a protein substance that stimulated wound healing. This substance was broken down and found to consist of Epithelial Growth Factor (EgF) which stimulates normal skin growth, Transforming Growth Factors (TgF), alpha and beta and Insulin Like Growth Factor (IgF-1) which stimulates cellular growth and repair"

Upon consideration of Clark et al's bibliography for the Sporn et al. reference (see Page 82) it provides a title referring to bovine colostrum – "Polypeptide Transforming Growth Factors (TGF A&B) and Epithelial Growth Factor Isolated from Bovine Colostrum Used for Wound Healing in Vivo". However, when sourcing the original article in the 1983 edition of "Science" magazine the actual reference and abstract do not refer to bovine colostrum (or EGF) at all. This is the actual reference, title and abstract from *Science* 18 March 1983: Vol. 219. no. 4590, pp. 1329 – 1331:

> "Polypeptide transforming growth factors isolated from bovine sources and used for wound healing in vivo" MB Sporn, *et al.* Transforming growth factors, which are polypeptides that induce the transformed phenotype in nonneoplastic cells, have been isolated in bulk amounts from bovine salivary gland and kidney. In experiments in which wound healing chambers were implanted subcutaneously in the backs of rats, these bovine transforming growth factors accelerated the accumulation of total protein, collagen, and DNA in treated chambers. These studies thus show an effect of an isolated transforming growth factor in vivo.

As can be seen the actual reference does not deal with bovine colostrum at all (the full paper is attached for reference).

With regards to the one reference to healing and IGF-1 on page 44 to 45 is *in vivo* (Sporn et al.) it relates an animal model situation where wound healing chambers were implanted subcutaneously in the backs of rats and TGF was used as the test substance and Applicants submit that this citation does not bear any relevance to the oral administration of bovine colostrum or to the putative effects of IGF-1. The results furthermore indicate the effect of TGF delivered systemically and deliberately absent the acidic environment of the GIT. Other references in this section of Clark et al. refer to *in-vitro* experiments and which are irrelevant to the present invention given that the conditions imposed in the GIT are very different to those as indicated on page 44 to 45 and again could not be expected to deliver sufficient quantities of IGF-1 to the cells through out the body because the exposure of IGF-1 in a culture is far different to that in the gut and would be furthermore diluted in a dairy composition when administered orally.

The Examiner also submits that Clark et al. discloses that colostrum is a food and promotes healing of the body composition by ridding the body of toxins and reducing fatigue. However the Applicants submit that at page 51 lines 1-3 Clark et al. discloses that colostrum may *cause an increase* in fatigue which teaches away from the present invention.

Finally the Examiner submits that Clark et al. discloses that colostrum reduces fatigue and infections that result from physical stress and hence extrapolates that this provides an improved exercise performance. In response Applicants submit that Clark et al. actually discloses exhaustive exercise increase both susceptibility to an severity of infections and that colostrum's many immune factors can reduce the infections caused by physical and emotional stress and that this is clearly not a disclosure of changing the physical work capacity of a subject.

Consequently, Applicants submit that there is no suggestion or motivation to modify the cited references or to combine reference teachings given that Clarke et al. is primarily directed to the

benefits of unprocessed colostrum and also (states that high percentages of immunoglobulin actually diminish colostrum's effectiveness see page 15). This teaches away from using any of the colostrum products produced in WO97/16977 and AU63136/94 since these two citations are concerned with processed colostrum and with increasing and preserving the antibody content so as to achieve a higher percentage of immunoglobulin.

Additionally, Applicants submit that given Clark et al teaches away from the use of colostrum containing higher percentages of immunoglobulin any combination with WO97/16977 and AU-A-63136/94 would only lead to an expectation that the composition prepared would not be effective and hence the combination of the cited art provides no reasonable expectation of success.

Furthermore, Clark et al. attempts to teach the involvement of IGF-1 in the mode of action of colostrum. However, the results in the present application (Example 2) show that there is no change in plasma IGF-1 concentration in response to bovine colostrum supplements, which confirms the theory that it is not possible to measure an increase in circulating IGF-1 from the oral administration of bovine colostrum. Due to this absence of change one would expect that the colostrum would have no effect on the body, particularly in the manner described by Clark et al. who emphasises the importance of IGF-1. Hence, if the results were considered then there would be no expectation of success as the IGF-1 concentration did not change by using the bovine colostrum supplements prepared according to the present invention.

Finally Applicants submit that even if the references are combined they do not provide a teaching of all the claimed limitations since contrary to the Examiner's submissions Clarke et al. does not disclose a change in the physical work capacity of a subject for the reasons discussed herein above.

Ballard et al. provides a disclosure of reconstituting freeze dried powder of colostrum and given that the present invention is directed to changing the physical work capacity of a subject the disclosure has been rendered moot.

Applicants submit that the methods claimed in this application are not obvious over the combination of references cited by the Examiner.

In view of the above, it is respectfully submitted that all rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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